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                 enhanced for more flexible patent number searching
                 CAS definition of basic patents expanded to ensure
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         AUG 27
                 comprehensive access to substance and sequence
                 information
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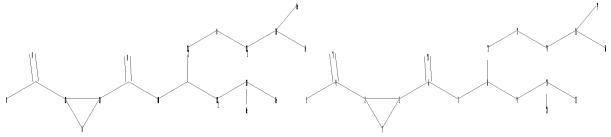
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chain nodes :

4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 ring nodes : 1 2 3

chain bonds :

 $2-4 \quad 3-6 \quad 4-5 \quad 4-17 \quad 6-7 \quad 6-18 \quad 7-8 \quad 8-9 \quad 8-12 \quad 9-10 \quad 10-11 \quad 10-20 \quad 12-13 \quad 13-14$ 

14-15 15-16 15-19

ring bonds : 1-2 1-3 2-3

exact/norm bonds :

1-2 1-3 2-3 4-5 4-17 6-7 6-18 7-8

exact bonds :

2-4 3-6 8-9 8-12 9-10 10-11 10-20 12-13 13-14 14-15 15-16 15-19

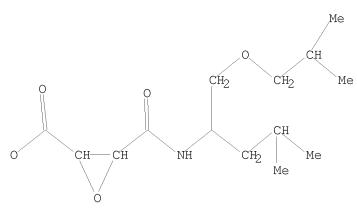
## Match level:

1:Atom 2:Atom 3:Atom 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS

## L1 STRUCTURE UPLOADED

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FULL SEARCH INITIATED 14:35:34 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 434 TO ITERATE

100.0% PROCESSED 19 ANSWERS 434 ITERATIONS

SEARCH TIME: 00.00.01

19 SEA SSS FUL L1

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ENTRY SESSION FULL ESTIMATED COST 179.74 179.95

FILE 'CAPLUS' ENTERED AT 14:35:41 ON 11 SEP 2008

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http://www.cas.org/legal/infopolicy.html

=> s 12

L3 4 L2

=> d 13 1-4 abs ibib hitstr

L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

AB The present invention relates to a method of using a therapeutically effective amount of at least one cathepsin B inhibitor for correcting bone mineralization defect. The invention also relates to a combination of the cathepsin B inhibitor with an other agent selected from the group of a second cathepsin B inhibitor, a PHEX polypoeptide, phosphate and calcitriol. Specifically, the invention discloses that the correction of bone miceralization defect includes an increase of d. of pure cortical bone, an increase of mean d. of tatal bone, an increase of cortical thickness, an increase of pure cortical area assigned to be cortical etc.

ACCESSION NUMBER: 2008:283346 CAPLUS

DOCUMENT NUMBER: 148:299923

TITLE: Methods of correcting bone mineralization defects by

using cathepsin B inhibitors and the kits and

compositions therefor

INVENTOR(S): Rowe, Peter; Yanagawa, Norimoto PATENT ASSIGNEE(S): The University of Kansas, USA

SOURCE: Can. Pat. Appl., 80pp.

CODEN: CPXXEB

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2558043	A1	20080224	CA 2006-2558043	20060824
AU 2006203680	A1	20080313	AU 2006-203680	20060824
PRIORITY APPLN. INFO.:			CA 2006-2558043	0 20060824
IT 791627-76-4				

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods of correcting bone mineralization defects by using cathepsin B inhibitors and kits and compns. therefor)

RN 791627-76-4 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (CA

INDEX NAME)

Absolute stereochemistry.

L3 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

AB Cathepsin K was originally identified as an osteoclast-specific lysosomal protease, the inhibitor of which has been considered might have therapeutic potential. We show that inhibition of cathepsin K could potently suppress autoimmune inflammation of the joints as well as osteoclastic bone resorption in autoimmune arthritis. Furthermore, cathepsin K-/- mice were resistant to exptl. autoimmune encephalomyelitis. Pharmacol. inhibition or targeted disruption of cathepsin K resulted in defective Toll-like receptor 9 signaling in dendritic cells in response to unmethylated CpG DNA, which in turn led to attenuated induction of T helper 17 cells, without affecting the antigen-presenting ability of dendritic cells. These results suggest that cathepsin K plays an important role in the immune system and may serve as a valid therapeutic target in autoimmune diseases.

ACCESSION NUMBER: 2008:126455 CAPLUS

DOCUMENT NUMBER: 148:306309

TITLE: Cathepsin K-Dependent Toll-Like Receptor 9 Signaling

Revealed in Experimental Arthritis

AUTHOR(S): Asagiri, Masataka; Hirai, Toshitake; Kunigami,

Toshihiro; Kamano, Shunya; Gober, Hans-Juergen; Okamoto, Kazuo; Nishikawa, Keizo; Latz, Eicke;

Golenbock, Douglas T.; Aoki, Kazuhiro; Ohya, Keiichi; Imai, Yuuki; Morishita, Yasuyuki; Miyazono, Kohei;

Kato, Shigeaki; Saftig, Paul; Takayanagi, Hiroshi
CORPORATE SOURCE: Department of Cell Signaling, Graduate School, Tokyo

Medical and Dental University, Tokyo, 113-8549, Japan

SOURCE: Science (Washington, DC, United States) (2008),

319 (5863), 624-627

CODEN: SCIEAS; ISSN: 0036-8075

PUBLISHER: American Association for the Advancement of Science

DOCUMENT TYPE: Journal LANGUAGE: English

IT 221144-20-3, NC 2300

RL: BUU (Biological use, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cathepsin K-dependent Toll-Like receptor 9 signaling revealed in exptl. arthritis)

RN 221144-20-3 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, sodium salt (1:1), (2S,3S)-(CA INDEX NAME)

Absolute stereochemistry.

Na

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

AΒ This invention is intended to purify (2S,3S)-3-[[(1S)-1-isobutoxymethyl-3-isobutoxmethylbutyl]carbamoyl]oxirane-2-carboxylic acid with the use of a salt from the carboxylic acid and an organic amine selected from among piperazine, adamantanamines, etc. and to provide crystalline sodium and potassium salts of the carboxylic acid which are enhanced in storage stability so as to be suitable for use as a raw material for medicinal drug. By this method, the title carboxylic acid was obtained in 99.9% purity.

ACCESSION NUMBER: 2004:965234 CAPLUS

DOCUMENT NUMBER: 141:410803

Process for preparation of (2S,3S)-3-[[(1S)-1-TITLE:

isobutoxymethyl-3-methylbutyl]carbamoyl]oxirane-2-

carboxylic acid salts

Tendo, Atsushi; Takahashi, Toshihiro; Yamakawa, Tomio; INVENTOR(S):

Okai, Kazuki; Nihashi, Susumu

Nippon Chemiphar Co., Ltd., Japan PATENT ASSIGNEE(S): SOURCE: PCT Int. Appl., 35 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.				KIND DATE		APPLICATION NO.						DATE						
WO	√O 2004096785				A1 20041111		WO 2004-JP5767					20040422						
	W:	ΑE,	AG,	AL,	ΑM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,	
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FΙ,	GB,	GD,	
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KΖ,	LC,	
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,	
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	
		ΤJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW	
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		BY,	KG,	KΖ,	MD,	RU,	ΤJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	
		ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	ΙΤ,	LU,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	
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		TD,	ΤG															
ΑU	2004	2342				AU 2004-234235					20040422							
CA	2523	233			A1 20041111		CA 2004-2523233						20040422					
ΕP	1619	190			A1 20060125			EP 2004-728921						20040422				
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CN	1809	549			A		2006	0726	(	CN 2	004-	8001	7044		2	0040	422	
US	20060252826 A1 200			2006	1109	US 2005-553946						20051021						

IN 2005CN02749 A 20070601 IN 2005-CN2749 20051024 PRIORITY APPLN. INFO.: JP 2003-121103 A 20030425 WO 2004-JP5767 W 20040422

IT 777838-84-3P 791627-71-9P 791627-72-0P 791627-73-1P 791627-74-2P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (intermediate; preparation of (2S,3S)-3-[[(1S)-1-isobutoxymethyl-3-

methylbutyl]carbamoyl]oxirane-2-carboxylic acid salts)

RN 777838-84-3 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, (2S,3S)- (CA INDEX NAME)

Absolute stereochemistry.

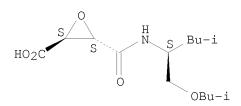
RN 791627-71-9 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, (2S,3S)-, compd. with cyclohexanamine (1:1) (CA INDEX NAME)

CM 1

CRN 777838-84-3 CMF C14 H25 N O5

Absolute stereochemistry.



CM 2

CRN 108-91-8 CMF C6 H13 N

RN 791627-72-0 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, (2S,3S)-, compd. with N1,N2-bis(phenylmethyl)-1,2-ethanediamine (1:1) (CA INDEX NAME)

CM 1

CRN 777838-84-3 CMF C14 H25 N O5

Absolute stereochemistry.

CM 2

CRN 140-28-3 CMF C16 H20 N2

 ${\tt Ph-CH_2-NH-CH_2-CH_2-NH-CH_2-Ph}$ 

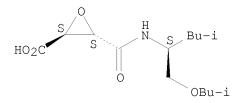
RN 791627-73-1 CAPLUS

CN D-Glucitol, 1-deoxy-1-(methylamino)-, (2S,3S)-3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]oxiranecarboxylate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 777838-84-3 CMF C14 H25 N O5

Absolute stereochemistry.



CM 2

CRN 6284-40-8 CMF C7 H17 N O5

RN 791627-74-2 CAPLUS

CN Lysine, mono[(2S,3S)-3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]oxiranecarboxylate] (9CI) (CA INDEX NAME)

CM 1

CRN 777838-84-3 CMF C14 H25 N O5

Absolute stereochemistry.

CM 2

CRN 70-54-2 CMF C6 H14 N2 O2

$$$^{\rm NH_2}_{\rm H_2N^-}$$$
 (CH<sub>2</sub>)  $_{\rm 4^-CH^-CO_2H}$ 

Absolute stereochemistry.

(CA INDEX NAME)

Na

RN 791627-75-3 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, potassium salt (1:1), (2S,3S)- (CA INDEX NAME)

Absolute stereochemistry.

K

RN 791627-77-5 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, (2S,3S)-, compd. with piperazine (1:1) (CA INDEX NAME)

CM 1

CRN 777838-84-3 CMF C14 H25 N O5

Absolute stereochemistry.

CM 2

CRN 110-85-0 CMF C4 H10 N2

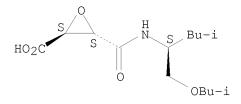
RN 791627-78-6 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, (2S,3S)-, compd. with tricyclo[3.3.1.13,7]decan-1-amine (1:1) (CA INDEX NAME)

CM 1

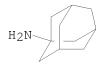
CRN 777838-84-3 CMF C14 H25 N O5

Absolute stereochemistry.



CM 2

CRN 768-94-5 CMF C10 H17 N



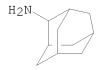
RN 791627-79-7 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, (2S,3S)-, compd. with tricyclo[3.3.1.13,7]decan-2-amine (1:1) (CA INDEX NAME)

CM 1

CRN 777838-84-3 CMF C14 H25 N O5

CRN 13074-39-0 CMF C10 H17 N



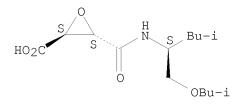
RN 791627-80-0 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, (2S,3S)-, compd. with N-cyclohexylcyclohexanamine (1:1) (CA INDEX NAME)

CM 1

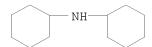
CRN 777838-84-3 CMF C14 H25 N O5

Absolute stereochemistry.



CM 2

CRN 101-83-7 CMF C12 H23 N



RN 791627-81-1 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, (2S,3S)-, compd. with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) (CA INDEX NAME)

CM 1

CRN 777838-84-3 CMF C14 H25 N O5

CM 2

CRN 77-86-1 CMF C4 H11 N O3

$$\begin{array}{c} ^{\rm NH_2} \\ ^{\rm HO-CH_2-C-CH_2-OH} \\ ^{\rm CH_2-OH} \end{array}$$

RN 791627-82-2 CAPLUS

CN L-Arginine, mono[(2S,3S)-3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]oxiranecarboxylate] (9CI) (CA INDEX NAME)

CM 1

CRN 777838-84-3 CMF C14 H25 N O5

Absolute stereochemistry.

CM 2

CRN 74-79-3 CMF C6 H14 N4 O2

Absolute stereochemistry.

IT 791627-76-4

RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of (2S,3S)-3-[[(1S)-1-isobutoxymethyl-3-methylbutyl]carbamoyl]oxirane-2-carboxylic acid salts)

RN 791627-76-4 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN GI

AΒ Novel epoxysuccinamide derivs. (3-carboxyoxirane-2-carboxamides) represented by general formula (I) or physiol. acceptable salts thereof [wherein R1 and R3 are each H, alkyl, alkenyl, alkynyl, aryl, aralkyl, a heterocyclic group, or alkyl substituted with a heterocyclic group; R2 is alkyl, alkenyl, alkynyl, aryl, aralkyl, a heterocyclic group, or alkyl substituted with a heterocyclic group; X is O or NR4 (wherein R4 is H, alkyl, aryl, aralkyl, a heterocyclic group, or alkyl substituted with a heterocyclic group); Y1 is OR5, SR6 or NR7R8 (wherein R5, R6 and R7 are each H, alkyl, aryl, aralkyl, acyl, a heterocyclic group, or alkyl substituted with a heterocyclic group; and R8 is the same as defined as to R4); and Y2 is H or alkyl, or alternatively Y1 and Y2 may be united to form =0, =S, =N-R9 or =N-OR10 (wherein R9 and R10 are each the same as defined as to R4), with the proviso that the alkyl, aryl and heterocyclic groups defined as to R5 to R10 may each have one or more specific substituents and that the groups defined as to R1 to R10 and Y2 are each specified in the number of carbon atoms] are prepared These compds. inhibit bone absorption and activity of cathepsin L and B (cysteine protease) and are useful for the treatment of bone diseases such as osteoporosis, malignant hypercalcemia, and Paget's disease of bone, arthritis deformans and chronic articular rheumatism accompanied by unusual exasperation of cathepsin B and L activity, and muscular dystrophy and muscular atrophy related to cathepsin B and L. Thus, (2S,3S)-3-ethoxycarbonyloxirane-2carboxylic acid was condensed with (S)-1-[(R)- $\alpha$ -methoxybenzyl]-3methylbutylamine using N-hydroxysuccinimide and DCC in EtOAc at room temperature

overnight to give the title compound (II). II at 15 mg/kg p.o. lowered

serum calcium by 20.4% in rat. ACCESSION NUMBER: 1999:184251 CAPLUS DOCUMENT NUMBER: 130:223163 Preparation of epoxysuccinamide derivatives for TITLE: treatment of bone diseases and arthritis INVENTOR(S): Nomura, Yutaka; Takahashi, Toshihiro; Yoshino, Yasushi; Nishioka, Koichiro PATENT ASSIGNEE(S): Nippon Chemiphar Co., Ltd., Japan SOURCE: PCT Int. Appl., 86 pp. CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: Japanese FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE \_\_\_\_ \_\_\_\_\_ \_\_\_\_\_\_ WO 9911640 A1 19990311 WO 1998-JP3983 19980904 W: AU, CA, CN, JP, KR, RU, US RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE EP 1022276 19990322 AU 1998-89978 19980904 20000723 20030528 A1 EP 1998-941728 19980904 EP 1022276 В1 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI AT 241607 20030615 AT 1998-941728 19980904 A2 EP 1342720 20030910 EP 2003-11154 19980904 EP 1342720 A3 20040211 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY L31324 T3 20040316 ES 1998-941728
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 PRIORITY APPLN. INFO.: OTHER SOURCE(S): MARPAT 130:223163 221144-15-6P 221144-16-7P 221144-17-8P 221144-18-9P 221144-19-0P 221144-20-3P RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of epoxysuccinamide derivs. as bone absorption inhibitors and cathepsin B and L inhibitors for treatment of bone diseases and arthritis)

221144-15-6 CAPLUS RN

2-Oxiranecarboxylic acid, 3-[[(1S)-3-methyl-1-[(2-methyl-1)-1]]]CN methylpropoxy)methyl]butyl]amino]carbonyl]-, 1-methylethyl ester, (2S,3S)-(CA INDEX NAME)

RN 221144-16-7 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, 1,1-dimethylethyl ester, (2S,3S)- (CA INDEX NAME)

Absolute stereochemistry.

RN 221144-17-8 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, cyclohexyl ester, (2S,3S)-(CA INDEX NAME)

Absolute stereochemistry.

RN 221144-18-9 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, phenyl ester, (2S,3S)- (CA INDEX NAME)

Absolute stereochemistry.

RN 221144-19-0 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-

methylpropoxy)methyl]butyl]amino]carbonyl]-, 4-(1,1-dimethylethyl)phenyl
ester, (2S,3S)- (CA INDEX NAME)

Absolute stereochemistry.

RN 221144-20-3 CAPLUS

CN 2-Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, sodium salt (1:1), (2S,3S)-(CA INDEX NAME)

Absolute stereochemistry.

Na

REFERENCE COUNT:

79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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